

A. Mohamed

CRF Errors Corrected by the STIC Systems Branch

Serial Number: 09/603,713

ENTERED

CRF Processing Date: 9/6/2001

Edited by: [signature]

Verified by: [signature]

(STIC stat)

☐ Changed a file from non-ASCII to ASCII

☐ Changed the margins in cases where the sequence text was "wrapped" down to the next line.

☐ Edited a format error in the Current Application Data section, specifically:

☐ Edited the Current Application Data section with the actual current number. The number inputted by the applicant was ☐ the prior application data; or ☐ other _____

☐ Added the mandatory heading and subheadings for "Current Application Data".

☐ Edited the "Number of Sequences" field. The applicant spelled out a number instead of using an integer.

☐ Changed the spelling of a mandatory field (the headings or subheadings), specifically:

☐ Corrected the SEQ ID NO when obviously incorrect. The sequence numbers that were edited were:

☐ Inserted or corrected a nucleic number at the end of a nucleic line. SEQ ID NO's edited:

☐ Corrected subheading placement. All responses must be on the same line as each subheading. If the applicant placed a response below the subheading, this was moved to its appropriate place.

☐ Inserted colons after headings/subheadings. Headings edited included:

☐ Deleted extra, invalid, headings-used by an applicant, specifically:

☐ Deleted: ☐ non-ASCII "garbage" at the beginning/end of files; ☐ secretary initials/filename at end of file;
☐ page numbers throughout text; ☐ other invalid text, such as _____

☐ Inserted mandatory headings, specifically:

☐ Corrected an obvious error in the response, specifically:

☐ Edited identifiers where upper case is used but lower case is required, or vice versa.

☐ Corrected an error in the Number of Sequences field, specifically:

☐ A "Hard Page Break" code was inserted by the applicant. All occurrences had to be deleted.

☐ Deleted ending stop codon in amino acid sequences and adjusted the "(A)Length:" field accordingly (error due to a PatentIn bug). Sequences corrected: _____

☒ Other:

Seq 31 - moved C2237 response up one line

Examiner: The above corrections must be communicated to the applicant in the first Office Action. DO NOT send a copy of this form.

3/1/95

RAW SEQUENCE LISTING

DATE: 09/06/2001

PATENT APPLICATION: US/09/603,713

TIME: 08:25:07

Input Set : A:\pto.amc.txt

Output Set: N:\CRF3\09062001\I603713.raw

P.5

3 <110> APPLICANT: Tang, Jordan J.N.
4 Hong, Lin
5 Ghosh, Arun K.
7 <120> TITLE OF INVENTION: Inhibitors of Memapsin 2 and Use Thereof
9 <130> FILE REFERENCE: OMRF 182
C--> 11 <140> CURRENT APPLICATION NUMBER: US/09/603,713
12 <141> CURRENT FILING DATE: 2000-06-27
14 <150> PRIOR APPLICATION NUMBER: 60/141,363
15 <151> PRIOR FILING DATE: 1999-06-28
17 <150> PRIOR APPLICATION NUMBER: 60/168,060
18 <151> PRIOR FILING DATE: 1999-11-30
20 <150> PRIOR APPLICATION NUMBER: 60/177,836
21 <151> PRIOR FILING DATE: 2000-01-25
23 <150> PRIOR APPLICATION NUMBER: 60/178,368
24 <151> PRIOR FILING DATE: 2000-01-27
26 <150> PRIOR APPLICATION NUMBER: 60/210,292
27 <151> PRIOR FILING DATE: 2000-06-08
29 <160> NUMBER OF SEQ ID NOS: 31
31 <170> SOFTWARE: PatentIn Ver. 2.1
33 <210> SEQ ID NO: 1
34 <211> LENGTH: 3252
35 <212> TYPE: DNA
36 <213> ORGANISM: Homo sapiens
38 <400> SEQUENCE: 1
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41 ccgggccgga ggggcagctt tgtggagatg gtggacaacc tgagggggcaa gtcggggcag 180
42 ggctactacg tggagatgac cgtgggcagc ccccgcgaga cgctcaacat cctgggtggat 240
43 acaggcagca gtaactttgc agtgggtgct gccccccacc ccttcctgca tcgctactac 300
44 cagaggcagc tgtccagcac ataccgggac ctccggaagg gtgtgtatgt gccctacacc 360
45 cagggcaagt gggaagggga gctgggcacc gacctggtaa gcatccccca tggccccaac 420
46 gtcactgtgc gtgccaacat tgcctgccatc actgaatcag acaagttctt catcaacggc 480
47 tccaactggg aaggcatcct ggggctggcc tatgctgaga ttgccaggcc tgacgactcc 540
48 ctggagcctt tctttgactc tctggtaaag cagaccacg ttcccaacct cttctccctg 600
49 cagctttgtg gtgctggctt cccccctaac cagtctgaag tgctggcctc tgcgaggagg 660
50 agcatgatca ttggaggtat cgaccactcg ctgtacacag gcagtctctg gtatacaccc 720
51 atccggcggg agtggtatta tgagggtgac attgtgcggg tggagatcaa tggacaggat 780
52 ctgaaaatgg actgcaagga gtacaactat gacaagagca ttgtggacag tggcaccacc 840
53 aaccttcgtt tgcccaagaa agtgtttgaa gctgcagtca aatccatcaa ggcagcctcc 900
54 tccacggaga agttccctga tggtttctgg ctaggagagc agctgggtgtg ctggcaagca 960
55 ggcaccaccc cttggaacat tttcccagtc atctcactct acctaatggg tgaggttacc 1020
56 aaccagtcct tccgcatcac catccttccg cagcaatacc tgcggccagt ggaagatgtg 1080
57 gccacgtccc aagacgactg ttacaagttt gccatctcac agtcatccac gggcactgtt 1140
58 atgggagctg ttatcatgga gggcttctac gttgtctttg atcgggcccg aaaacgcaatt 1200
59 ggctttgctg tcagcgcttg ccatgtgcac gatgagttca ggacggcagc ggtggaaggc 1260
60 ccttttgtca ccttgacat ggaagactgt ggctacaaca ttccacagac agatgagtca 1320
61 accctcatga ccatagccta tgtcatggct gccatctgcg ccctcttcat gctgccactc 1380

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Input Set : A:\pto.amc.txt

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62 tgcctcatgg tgtgtcagtg gcgctgcctc cgctgcctgc gccagcagca tgatgacttt 1440
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64 ggaccacacc tccgtgggtc actttgttca caagtaggag acacagatgg cacctgtggc 1560
65 cagagcacct caggaccctc cccaccacc aaatgcctct gccttgatgg agaaggaaaa 1620
66 ggctggcaag gtgggttcca gggactgtac ctgtaggaaa cagaaaagag aagaaaagag 1680
67 cactctgctg gcggaatac tcttggtcac ctcaaattta agtcgggaaa ttctgctgct 1740
68 tgaacttca gccctgaacc ttgtccacc attcctttaa attctccaac ccaaagtatt 1800
69 cttcttttct tagtttcaga agtactggca tcacacgcag gttaccttgg cgtgtgtccc 1860
70 tgtggtaccc tggcagagaa gagaccaagc ttgtttccct gctggccaaa gtcagtagga 1920
71 gaggatgcac agtttgcata ttgctttaga gacagggaact gtataaacia gcctaaccatt 1980
72 ggtgcaaaga ttgcctcttg aattaaiaaa aaactagatt gactatttat acaaagggg 2040
73 gcggctggaa agaggagaag gagaggagat acaaagacag ggaatagtgg gatcaaagct 2100
74 aggaaaggca gaaacacaac cactcaccag tcctagtatt agacctcatc tccaagatag 2160
75 catcccatct cagaagatgg gtgtgtttt caatgttttc ttttctgtgg ttgcagcctg 2220
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83 agtagcaaga tctttacata attcagagtg gtttcattgc ctctctacc tctctaattg 2700
84 cccctccatt tatttgacta aagcatcrca cagtggcact agcattatac caagagtatg 2760
85 agaaatacag tgctttatgg ctctaactt actgccttca gtatcaaggc tgctggaga 2820
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88 gctggttctt gggctaggtg gtggggacca agttcattac ctccctatca gttctagcat 3000
89 agtaactac ggtaccagtg ttagtgggaa gagctgggtt ttcctagtat acccactgca 3060
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91 acctgataag ggagagggaa atacaaggag ggcctctggt gttcctggcc tcagccagct 3180
92 gccmcaagc cataaaccaa taaamcaaga atactgagtc taiaiaiaia aiaiaiaia 3240
93 aiaiaiaia aa 3252
96 <210> SEQ ID NO: 2
97 <211> LENGTH: 488
98 <212> TYPE: PRT
99 <213> ORGANISM: Homo sapiens
101 <220> FEATURE:
102 <223> OTHER INFORMATION: Purified Memapsin 2
104 <220> FEATURE:
105 <223> OTHER INFORMATION: Amino Acids 28-48 are remnant putative propeptide
106 residues
108 <220> FEATURE:
109 <223> OTHER INFORMATION: Amino Acids 58-61, 78, 80, 82-83, 116, 118-121,
110 156, 166, 174, 246, 274, 276, 278-281, 283, and
111 376-377 are residues in contact with the OM99-2
112 inhibitor
114 <220> FEATURE:
115 <223> OTHER INFORMATION: Amino acids 54-57, 61-68, 73-80, 86-89, 109-111,
116 113-118, 123-134, 143-154, 165-168, 198-202, and

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RAW SEQUENCE LISTING

DATE: 09/06/2001

PATENT APPLICATION: . US/09/603,713

TIME: 08:25:07

Input Set : A:\pto.amc.txt

Output Set: N:\CRF3\09062001\I603713.raw

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117      220-224 are N-lobe Beta Strands
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120 <223> OTHER INFORMATION: Amino Acids 184-191 and 210-217 are N-lobe Helices
122 <220> FEATURE:
123 <223> OTHER INFORMATION: Amino acids 237-240, 247-249, 251-256, 259-260,
124      273-275, 282-285, 316-318, 331-336, 342-348,
125      354-357, 366-370, 372-375, 380-383, 390-395,
126      400-405, and 418-420 are C-lobe Beta Strands
128 <220> FEATURE:
129 <223> OTHER INFORMATION: Amino Acids 286-299, 307-310, 350-353, 384-387,
130      and 427-431 are C-lobe Helices
132 <400> SEQUENCE: 2
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134   1          5          10          15
136 Leu Arg Ser Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg
137          20          25          30
139 Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val
140          35          40          45
142 Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val
143          50          55          60
145 Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp
146          65          70          75          80
148 Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu
149          85          90          95
151 His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg
152          100          105          110
154 Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu
155          115          120          125
157 Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg
158          130          135          140
160 Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly
161 145          150          155          160
163 Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg
164          165          170          175
166 Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr
167          180          185          190
169 His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro
170          195          200          205
172 Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile
173          210          215          220
175 Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro
176 225          230          235          240
178 Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile
179          245          250          255
181 Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys
182          260          265          270
184 Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val
185          275          280          285
187 Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys

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Input Set : A:\pto.amc.txt

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188      290      295      300
190 Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala
191 305      310      315      320
193 Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met
194      325      330      335
196 Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln
197      340      345      350
199 Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr
200      355      360      365
202 Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val
203      370      375      380
205 Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile
206 385      390      395      400
208 Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala
209      405      410      415
211 Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr
212      420      425      430
214 Asn Ile Pro Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val
215      435      440      445
217 Met Ala Ala Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val
218      450      455      460
220 Cys Gln Trp Arg Cys Leu Arg Cys Leu Arg Gln Gln His Asp Asp Phe
221 465      470      475      480
223 Ala Asp Asp Ile Ser Leu Leu Lys
224      485
227 <210> SEQ ID NO: 3
228 <211> LENGTH: 503
229 <212> TYPE: PRT
230 <213> ORGANISM: Homo sapiens
232 <220> FEATURE:
233 <223> OTHER INFORMATION: Pro-memapsin 2
235 <220> FEATURE:
236 <223> OTHER INFORMATION: Amino Acids 1-15 are vector-derived residues
238 <220> FEATURE:
239 <223> OTHER INFORMATION: Amino Acids 16-64 are a putative pro peptide
241 <220> FEATURE:
242 <223> OTHER INFORMATION: Amino Acids 1-13 are the T7 promoter
244 <220> FEATURE:
245 <223> OTHER INFORMATION: Amino Acids 16-456 are Pro-memapsin 2-T1
247 <220> FEATURE:
248 <223> OTHER INFORMATION: Amino Acids 16-421 are Promemapsin 2-T2
250 <400> SEQUENCE: 3
251 Met Ala Ser Met Thr Gly Gly Gln Gln Met Gly Arg Gly Ser Met Ala
252 1      5      10      15
254 Gly Val Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu
255      20      25      30
257 Arg Ser Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu
258      35      40      45
260 Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu

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Output Set: N:\CRF3\09062001\I603713.raw

261	50					55				60						
263	Met	Val	Asp	Asn	Leu	Arg	Gly	Lys	Ser	Gly	Gln	Gly	Tyr	Tyr	Val	Glu
264	65					70				75					80	
266	Met	Thr	Val	Gly	Ser	Pro	Pro	Gln	Thr	Leu	Asn	Ile	Leu	Val	Asp	Thr
267					85					90					95	
269	Gly	Ser	Ser	Asn	Phe	Ala	Val	Gly	Ala	Ala	Pro	His	Pro	Phe	Leu	His
270				100					105					110		
272	Arg	Tyr	Tyr	Gln	Arg	Gln	Leu	Ser	Thr	Tyr	Arg	Asp	Leu	Arg	Lys	
273			115					120				125				
275	Gly	Val	Tyr	Val	Pro	Tyr	Thr	Gln	Gly	Lys	Trp	Glu	Gly	Glu	Leu	Gly
276		130					135					140				
278	Thr	Asp	Leu	Val	Ser	Ile	Pro	His	Gly	Pro	Asn	Val	Thr	Val	Arg	Ala
279	145					150					155				160	
281	Asn	Ile	Ala	Ala	Ile	Thr	Glu	Ser	Asp	Lys	Phe	Phe	Ile	Asn	Gly	Ser
282					165					170					175	
284	Asn	Trp	Glu	Gly	Ile	Leu	Gly	Leu	Ala	Tyr	Ala	Glu	Ile	Ala	Arg	Pro
285				180					185					190		
287	Asp	Asp	Ser	Leu	Glu	Pro	Phe	Phe	Asp	Ser	Leu	Val	Lys	Gln	Thr	His
288			195						200				205			
290	Val	Pro	Asn	Leu	Phe	Ser	Leu	Gln	Leu	Cys	Gly	Ala	Gly	Phe	Pro	Leu
291		210					215					220				
293	Asn	Gln	Ser	Glu	Val	Leu	Ala	Ser	Val	Gly	Gly	Ser	Met	Ile	Ile	Gly
294	225					230					235				240	
296	Gly	Ile	Asp	His	Ser	Leu	Tyr	Thr	Gly	Ser	Leu	Trp	Tyr	Thr	Pro	Ile
297				245						250					255	
299	Arg	Arg	Glu	Trp	Tyr	Tyr	Glu	Val	Ile	Ile	Val	Arg	Val	Glu	Ile	Asn
300				260					265					270		
302	Gly	Gln	Asp	Leu	Lys	Met	Asp	Cys	Lys	Glu	Tyr	Asn	Tyr	Asp	Lys	Ser
303			275					280					285			
305	Ile	Val	Asp	Ser	Gly	Thr	Thr	Asn	Leu	Arg	Leu	Pro	Lys	Lys	Val	Phe
306		290					295					300				
308	Glu	Ala	Ala	Val	Lys	Ser	Ile	Lys	Ala	Ala	Ser	Ser	Thr	Glu	Lys	Phe
309	305					310					315				320	
311	Pro	Asp	Gly	Phe	Trp	Leu	Gly	Glu	Gln	Leu	Val	Cys	Trp	Gln	Ala	Gly
312				325					330						335	
314	Thr	Thr	Pro	Trp	Asn	Ile	Phe	Pro	Val	Ile	Ser	Leu	Tyr	Leu	Met	Gly
315				340					345					350		
317	Glu	Val	Thr	Asn	Gln	Ser	Phe	Arg	Ile	Thr	Ile	Leu	Pro	Gln	Gln	Tyr
318			355					360					365			
320	Leu	Arg	Pro	Val	Glu	Asp	Val	Ala	Thr	Ser	Gln	Asp	Asp	Cys	Tyr	Lys
321		370					375					380				
323	Phe	Ala	Ile	Ser	Gln	Ser	Ser	Thr	Gly	Thr	Val	Met	Gly	Ala	Val	Ile
324	385				390						395				400	
326	Met	Glu	Gly	Phe	Tyr	Val	Val	Phe	Asp	Arg	Ala	Arg	Lys	Arg	Ile	Gly
327				405					410					415		
329	Phe	Ala	Val	Ser	Ala	Cys	His	Val	His	Asp	Glu	Phe	Arg	Thr	Ala	Ala
330				420					425					430		
332	Val	Glu	Gly	Pro	Phe	Val	Thr	Leu	Asp	Met	Glu	Asp	Cys	Gly	Tyr	Asn
333			435					440					445			

Use of n and/or Xaa has been detected in the Sequence Listing.
 Review the Sequence Listing to insure a corresponding
 explanation is presented in the <220> to <223> fields of
 each sequence using n or Xaa.



VERIFICATION SUMMARY

DATE: 09/06/2001

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Input Set : A:\pto.amc.txt

Output Set: N:\CRF3\09062001\I603713.raw

L:11 M:270 C: Current Application Number differs, Replaced Current Application Number
L:580 M:258 W: Mandatory Feature missing, <221> not found for SEQ ID#:22
L:580 M:258 W: Mandatory Feature missing, <222> not found for SEQ ID#:22
L:580 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:22
L:597 M:258 W: Mandatory Feature missing, <221> not found for SEQ ID#:23
L:597 M:258 W: Mandatory Feature missing, <222> not found for SEQ ID#:23
L:597 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:23